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Vista IP Law Group LLP
2040 MAIN STREET, Suite 710
IRVINE, CA 92614

EXAMINER	
WOOLWINE, SAMUEL C	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/582,393	KRANEWITTER ET AL.	
	Examiner	Art Unit	
	SAMUEL C. WOOLWINE	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29,30 and 70-95* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29,30 and 70-95* is/are rejected.

7)☒ Claim(s) *29 and 87* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 June 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :06/09/2006, 01/11/2007, 08/18/2009.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group II, claims 29-30, in the reply filed on 12/22/2009 is acknowledged.

Claims 1-3, directed to a non-elected invention, have been cancelled.

New claims 70-95 have been added.

Applicant's election of SEQ ID NO:8 in response to the requirement for election of species is noted (see Applicant's response filed 04/06/2010).

Drawings

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because the drawings submitted as part of the original international application PCT/EP2004/013879 have non-English text (see the published Application, US 2008/0287318). Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Objections

Claims 29 and 87 are objected to as being of improper Markush form. As discussed at MPEP 2173.05(h) (see first paragraph):

"Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of

alternative expression, which is commonly referred to as a Markush group, recites members as being "selected from the group consisting of A, B and C." See *Ex parte Markush*, 1925 C.D. 126 (Comm'r Pat. 1925)."

However, see second paragraph:

"It is improper to use the term "comprising" instead of "consisting of." *Ex parte Dotter*, 12 USPQ 382 (Bd. App. 1931)."

Claims 29 and 87 each recites "selected from the group comprising...", the latter claim having two such instances (one just prior to section (a), another in section (c)). Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30, 71, 73, 76, 79, 82, 85 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 30, the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Moreover, it is unclear what dimensions are required by the phrase "stated in the recommendations of the SBS (Society of Biomolecular Screening)". This latter issue also serves as the basis for rejection of these same claims under 35 USC 112, 1st paragraph (see below).

Because claims 71, 73, 76, 79, 82, 85 ultimately depend from claim 30, they are rejected for the same reason.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30, 71, 73, 76, 79, 82, 85 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The dimensions critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). Specifically, dimensions are required by the phrase "stated in the recommendations of the SBS (Society of Biomolecular Screening)", but the disclosure does not provide what these dimensions are. The limitation amounts to an incorporation by reference. However, even if some document existed, published by the Society of Biomolecular Screening, with "recommended" dimensions, the incorporation by reference of essential material is prohibited. See 37 CFR 1.57(c):

"Essential material" may be incorporated by reference, but only by way of an incorporation by reference to a U.S. patent or U.S. patent application publication, which patent or patent application publication does not itself incorporate such essential material by reference. "Essential material" is material that is necessary to:

(1) Provide a written description of the claimed invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and set forth

the best mode contemplated by the inventor of carrying out the invention as required by the first paragraph of 35 U.S.C. 112;

(2) Describe the claimed invention in terms that particularly point out and distinctly claim the invention as required by the second paragraph of 35 U.S.C. 112; or

(3) Describe the structure, material, or acts that correspond to a claimed means or step for performing a specified function as required by the sixth paragraph of 35 U.S.C. 112.

Because claims 71, 73, 76, 79, 82, 85 ultimately depend from claim 30, they are rejected for the same reason.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 29, 30, 70-80, 94 and 95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thunnissen et al (WO 03/087829, cited on the IDS of 08/18/2009) in

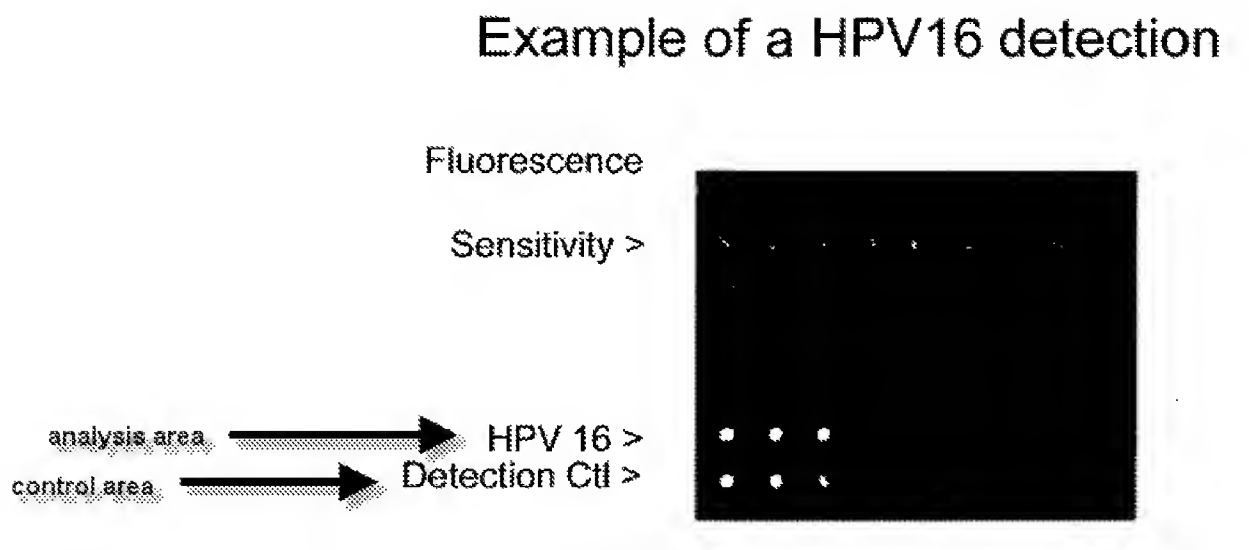
view of GenBank GI:60955 [online] July 6, 1989 [retrieved on July 3, 2010] retrieved from:

http://www.ncbi.nlm.nih.gov/sviewer/viewer.fcgi?val=60955&sat=OLDID&satkey=34726

With regard to claim 29, Thunnissen taught a nucleotide array for detecting and/or identifying the genotype of a human papilloma virus, the array comprising a solid carrier (support) and HPV-specific capture probes designed to hybridize with the E1 gene of HPV (see abstract, figure 2, page 4 [lines 10-11 and 23-29], page 5 [line 32] through page 6 [line 2], pages 9-10 and Table 1). Thunnissen also taught the probes used could be complementary to the sequences shown in the table (page 12, lines 27-28).

With regard to claim 30, Thunnissen taught the solid support of the array could be in the form of a microscope slide (page 9, lines 10-11, for example).

With regard to claims 70 and 71, Thunnissen's array had HPV-specific capture probes in a "defined analysis area" (see figure 3). With regard to claims 72-74, Thunnissen's array had a "control area" (see figure 3):



With regard to claims 75-80 and 94 Thunnissen taught (page 12, lines 23-26): "For purposes of recognition the [*sic*] where the spots are located on the slide we used marker oligonucleotides with a 5' biotin-modified oligonucleotides of 40 nucleotides in length with a digoxigenin-modification at the penultimate 3' terminal nucleotide." See also page 13, lines 29-34. That is, Thunnissen's array comprised additional oligonucleotides serving as a control for orientation. Note, however, that the same oligonucleotides could *also* serve the purpose of being a print control (since these oligonucleotides were printed on the array).

With regard to claim 94, which use the terms "sixth oligonucleotide", it is noted that the claim depends from claim 75, which recites the various controls in an "and/or" manner. Therefore, claim 94 simply requires a "print control". That is, the term "sixth" is not construed as requiring the presence of a "second", "third", "fourth" or "fifth" oligonucleotide on the array. Hence, claim 94 requires an array with at least one "first"

oligonucleotide (i.e. the HPV genotyping probe) and an additional oligonucleotide serving as a print control.

With regard to claim 95, Thunnissen taught that the probes could be DNA (page 10, lines 1-5) or PNA (page 12, lines 20-22).

Thunnissen did not teach or suggest an HPV-specific probe having the sequences of SEQ ID NO:8.

GenBank GI:60955 disclosed the sequence of HPV type 6, in which the sequence of SEQ ID NO:8 appears:

```
>gi|60955|emb|X00203.1|  Genital human papillomavirus type 6b (HPV6b)
Length=7902

 Score = 60.0 bits (30),  Expect = 3e-07
 Identities = 30/30 (100%), Gaps = 0/30 (0%)
 Strand=Plus/Plus

Query  1     AAGCTTTCTAGGAGGTACAGTTATTAGTCA  30
             ||||||||||||||||||||||||||||||
Sbjct  2307  AAGCTTTCTAGGAGGTACAGTTATTAGTCA  2336
```

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to choose alternative sequences from the E1 gene unique to particular HPV subtypes for use as probes instead of or in addition to the E1 gene probes disclosed by Thunnissen. One of ordinary skill would have realized that any sequence of the E1 gene that was unique to a particular HPV type could be used as a specific probe for that HPV type. Moreover, as indicated by Thunnissen's disclosure (e.g. page 12, lines 11-17), the sequences of the E1 genes from enough HPV types were known in order to allow one of skill in the art to follow the well-known procedure of aligning homologous sequences from related organisms, finding regions where the

sequences differed, and using those regions to select probes that distinguish one sequence (and thus HPV type) from another.

Claims 81-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thunnissen et al (WO 03/087829, cited on the IDS of 08/18/2009) in view of GenBank GI:60955 [online] July 6, 1989 [retrieved on July 3, 2010] retrieved from: http://www.ncbi.nlm.nih.gov/sviewer/viewer.fcgi?val=60955&sat=OLDID&satkey=34726 as applied to claims 29, 30, 70-80, 94 and 95 above, and further in view of Amundson et al (WO 00/50643).

The teachings of Thunnissen and GenBank have been discussed. These references did not teach or suggest that an additional oligonucleotide (i.e. other than an HPV type-specific probe) included on the array was a fluorescent oligonucleotide (Thunnissen's orientation control was labeled with digoxigenin, which was visualized with an alkaline phosphatase detection reaction; however the oligonucleotide itself was not fluorescently labeled). Nor did Thunnissen teach at least three spots of the fluorescently labeled oligonucleotide.

Amundson taught a microarray for detecting characteristic changes in gene expression patterns following exposure to radiation (see abstract). Amundson taught the probes could be oligonucleotides (page 2, lines 9-11). Amundson also taught at least three spots of DNA labeled *prior to printing on the array* to serve as orientation markers for a computerized scanner (page 5, lines 32-42 and figure 4).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the arrays suggested by the combined teachings of Thunnissen and GenBank to include fluorescently labeled oligonucleotides as orientation controls, as suggested by Amundson. Although Thunnissen taught orientation control probes labeled with digoxigenin, which were visualized with an alkaline phosphatase detection reaction, he also expressly contemplated other visualization platforms, including fluorescent substances (page 15, lines 24-32). One of ordinary skill would have understood that the fluorescently-labeled orientation probes taught by Amundson would have been a suitable alternative to the digoxigenin-labeled probes taught by Thunnissen.

Claims 84-86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thunnissen et al (WO 03/087829, cited on the IDS of 08/18/2009) in view of GenBank GI:60955 [online] July 6, 1989 [retrieved on July 3, 2010] retrieved from: http://www.ncbi.nlm.nih.gov/sviewer/viewer.fcgi?val=60955&sat=OLDID&satkey=34726 and Amundson et al (WO 00/50643) as applied to claims 81-83 above, and further in view of Fodor et al (US 2003/0186296).

The teachings of Thunnissen, GenBank and Amundson have been discussed. These references did not teach or suggest an array having, in addition to an HPV typing probe and orientation probe, an amplification probe.

Fodor taught (paragraph [0148]): "The high density array may also include sample preparation/amplification control probes. These are probes that are

complementary to subsequences of control genes selected because they do not normally occur in the nucleic acids of the particular biological sample being assayed."

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the array suggested by the combined teachings of Thunnissen, GenBank and Amundson to include amplification control probes as suggested by Fodor, for the obvious reason of detecting false negative results due to failure of the amplification reaction (e.g. due to defective polymerase preparation, improper reaction conditions, the presence of substances inhibitory to the amplification reaction, etc).

Claims 87 and 88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thunnissen et al (WO 03/087829, cited on the IDS of 08/18/2009) in view of GenBank GI:60955 [online] July 6, 1989 [retrieved on July 3, 2010] retrieved from: http://www.ncbi.nlm.nih.gov/sviewer/viewer.fcgi?val=60955&sat=OLDID&satkey=3472, Amundson et al (WO 00/50643) and Fodor et al (US 2003/0186296) as applied to claims 84-86 above, and further in view of Walkerpeach et al (US 2001/0006800).

The teachings of Thunnissen, GenBank, Amundson and Fodor have been discussed. The effect of the language of claim 87, so far as the examiner can tell, requires that the "third oligonucleotide" of the array (i.e. the amplification control probe), must be "suitable" for detecting an amplification of a "control nucleic acid" (which is not specified by the claim), and that the "control nucleic acid" must be capable of being amplified by primers as recited in sections (a) through (f) of the claim. It appears that

the intent is to design a control nucleic acid that can be amplified by the same primers used to amplify the portion of the HPV E1 gene which is to be detected by the HPV typing probe. This is not taught or suggested by the cited references.

Walkerpeach taught (paragraph [0018]): "The present invention relates to methods and compositions that provide a positive control to identify inhibition during a signal amplification reaction."

Walkerpeach taught (paragraph [0025], emphasis provided): "The present invention contemplates utility for use as an internal inhibition control in a variety of signal amplification assays. Examples of signal amplification assays include: the polymerase chain reaction (PCR), variations of PCR, including reverse transcriptase PCR, real-time PCR, branched DNA (bDNA) assays, nucleic acid sequence based amplification assays (NASBA), transcription mediated amplification (TMA), cytoflowmetric assays, molecular beacon assays, hydridization reactions, and detection assays."

Walkerpeach taught (paragraph [0026], emphasis provided): "The internal control cassette (ICC) may consist of any target sequence that may be amplified by PCR or other nucleotide amplification techniques. Sequences that are present in clinically important disease states are particularly relevant to the present invention. Examples provided for illustrative purposes include sequences from viruses such as human immunodeficiency virus (HIV), herpes simplex virus (HSV), hepatitis C virus (HCV), human papilloma virus (HPV), and cytomegalovirus (CMV)."

Walkerpeach taught (paragraph [0026]): "The ICC advantageously comprises a target sequence with an internal segment in an inverted orientation, with respect to the target sequence as it appears in nature, and one or more primer binding sites. The segment of sequence inverted in the ICC preferably lies immediately adjacent to or is flanked by the amplification primer binding site or sites that are used to amplify the experimental target sequence."

Walkerpeach taught (paragraph [0033]): "The present method differs from those methods of the prior art in that it uses the same sequence as the target in the internal control construct, although an internal segment is inverted. By using an inverted sequence of a proposed target, as opposed to a randomly generated control sequence, the present invention creates a control sequence that shares many of the same biochemical characteristics of the target sequence (e.g., reaction kinetics, temperature of melting (T_M), and nucleotide composition)."

Walkerpeach taught (paragraph [0034]): "One shared feature is that the same primers may be used to amplify both the control and target sequences. When the same primer pair is used for both sequences, the hybridization or primer annealing conditions for both the experimental and ICC control sequences are the same. Thus, using the same primers and primer binding sites for both sequences eliminates another variable which might effect the signal produced from the control and target sequences."

That is, Walkerpeach's idea was to make a control nucleic acid by taking the experimental target that was to be analyzed, and "flipping" an internal segment thereof, such that the target and control nucleic acid could be amplified by the same primer pair,

yet generate amplicons having distinguishable sequences. Importantly, however, this would generate an amplification product of the control nucleic acid having similar properties to the amplification product of the experimental target (e.g. melting temperature, nucleotide content, etc).

Furthermore, Walkerpeach taught detecting each amplification product (derived from the experimental target and the amplification control or ICC) using corresponding capture probes immobilized in separate wells of a microtiter plate (i.e. an "array"). See Example 3 beginning at paragraph [0066] and see figure 1.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the array suggested by the combined teachings of Thunnissen, GenBank, Amundson and Fodor by constructing a control nucleic acid and corresponding capture probe (i.e. amplification control probe) as suggested by Walkerpeach, such that the control nucleic acid was the same as the target nucleic acid but for an internal segment in reversed orientation relative to the experimental target. One would have been motivated to do so because Walkerpeach explains several advantages derived by this approach at paragraphs [0036]-[0041]: it provides a number of quantitative similarities between the sequences that improves the significance of the inhibition control. For example, reaction parameters such as the T_M, the length of the sequence amplified, primer annealing or hybridization and primer usage are all substantially the same for the experimental and control sequences. Thus, the inverted sequence of the control provides "an extremely valid method for investigators to monitor for inhibition during signal amplification reactions" (paragraph [0036]).

By following the method outlined by Walkerpeach, one would have been lead to construct a control nucleic acid that was the same as the target (in the instant situation, a segment of the HPV E1 gene) except for an inverted segment between the primer binding sites. One would also have designed a probe to detect the amplification product of the control nucleic acid that was complementary to this inverted segment, as shown in Walkerpeach's figure 1. In doing this, one would have arrived at the array of claims 87 and 88 since (for claim 87), the array would contain a probe suitable for detecting an amplification product of a control nucleic acid, which control nucleic could be amplified using the same primers as used for the target HPV sequence, and (for claim 88), the control nucleic acid would inherently have a length and GC content corresponding to the HPV target sequence being amplified (see Walkerpeach, paragraphs [0033], [0036], [0041]).

It is noted, with respect to the limitations recited in claim 87 regarding the primers used, that these limitations only serve to structurally define the claimed array by requiring that the amplification control probe must be suitable to detect the amplification product of a control nucleic acid that *could be amplified* by such primers. However, an array having (1) an HPV typing probe of SEQ ID NO:8 (suggested by the combined teachings of Thunnissen and GenBank), (2) an amplification control probe having a sequence being the *reverse* of SEQ ID NO:8 (arrived at by following the technique of Walkerpeach), and (3) an fluorescently-labeled orientation control probe (required by indirect dependency from claim 81, and as suggested by the combined teachings of Thunnissen and Amundson) would meet the *structural* limitations of the claim, since an

amplification product of the HPV E1 gene *could* be amplified with the primers of claim 87 and detected by SEQ ID NO:8 (assuming the HPV in the sample were HPV type 6), and a control nucleic acid identical to the amplified portion of the HPV 6 E1 gene segment but for a reversed internal segment *could be constructed* such that it *could be amplified* by the primers recited in claim 87.

Claims 89-91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thunnissen et al (WO 03/087829, cited on the IDS of 08/18/2009) in view of GenBank GI:60955 [online] July 6, 1989 [retrieved on July 3, 2010] retrieved from: http://www.ncbi.nlm.nih.gov/sviewer/viewer.fcgi?val=60955&sat=OLDID&satkey=34726 as applied to claims 29, 30, 70-80, 94 and 95 above, and further in view of Sabath et al (US 2003/0175761).

The teachings of Thunnissen and GenBank have been discussed. These references did not teach or suggest a hybridization control comprised of an oligonucleotide or nucleic acid (as recited in claim 89), wherein the hybridization comprised at least 2-10 spots with various amounts of the oligonucleotide or nucleic acid (as recited in claim 90), wherein the spots comprise a "dilution series" (as recited in claim 91).

Sabath taught (paragraph [0038]): "Arrays of this invention may contain control probes as well as probes for genes. Controls that can be included on the arrays of this invention include hybridization controls and scanning controls. The controls can be positive or negative controls. One type of hybridization control is spotting the same

probe for a gene several times on one chip, each spot having different amounts of probe. This allows for the amount of probe of a given sequence to be optimized."

Sabath's term "several" would have implied at least two spots. In addition, any two spots, each having a different amount of probe, could be considered a "dilution series".

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the array suggested by the combined teachings of Thunnissen and GenBank by including on the a hybridization control comprised of "several" spots of a probe at various concentrations as suggested by Sabath, since this was apparently a known control to use on microarrays, and in addition Sabath taught this allowed one to optimize the amount of probe for any given sequence.

Claim 92 is rejected under 35 U.S.C. 103(a) as being unpatentable over Thunnissen et al (WO 03/087829, cited on the IDS of 08/18/2009) in view of GenBank GI:60955 [online] July 6, 1989 [retrieved on July 3, 2010] retrieved from: http://www.ncbi.nlm.nih.gov/sviewer/viewer.fcgi?val=60955&sat=OLDID&satkey=34726 as applied to claims 29, 30, 70-80, 94 and 95 above, and further in view of Neefe et al (US 2003/0170268).

The teachings of Thunnissen and GenBank have been discussed. These references did not teach or suggest a "sample control".

Neefe taught determining HPV type by taking samples from human patients, amplifying with HPV consensus primers and probing with HPV type specific probes

(paragraph [0072]). Neefe also taught amplifying these same samples with primers to beta-globin, a human gene, and probing with a beta-globin probe as a control to ensure that the amplification was successful (paragraph [0073]).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the array suggested by the combined teachings of Thunnissen and GenBank by including a probe for beta-globin, so that one could co-amplify the sample with beta-globin primers and thereby ensure that the amplification was successful. Although Neefe referred to this as a control for "amplification", the term "amplification control" and "sample control" do not structurally distinguish over an array comprising an HPV typing probe and a beta-globin probe.

Claim 93 is rejected under 35 U.S.C. 103(a) as being unpatentable over Thunnissen et al (WO 03/087829, cited on the IDS of 08/18/2009) in view of GenBank GI:60955 [online] July 6, 1989 [retrieved on July 3, 2010] retrieved from: http://www.ncbi.nlm.nih.gov/sviewer/viewer.fcgi?val=60955&sat=OLDID&satkey=34726 and Neefe et al (US 2003/0170268) as applied to claim 92 above, and further in view of Maas et al (PNAS 96:8895-8900, August 1999).

The teachings of Thunnissen, GenBank and Neefe have been discussed. These references did not teach or suggest the use of human ADAT1 as a control in place of beta-globin.

Maas determined the sequence of human ADAT1 cDNA and disclosed human ADAT1 specific primers (page 8896, column 2, third paragraph). Maas also deposited

the ADAT1 sequence in a public database (as GenBank accession number AF125188; see page 8895, column 2, footnote).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the beta-globin specific probe suggested by Neefe with a human ADAT1 specific probe (and, of course, to use human ADAT1 specific primers in place of beta-globin specific primers), since one of ordinary skill in the art would have understood that *any* human DNA sequence could have been substituted for beta-globin, since the whole purpose of the control suggested by Neefe was to ensure that nucleic acid could be amplified from a human sample. One of ordinary skill in the art would have understood that any known human DNA sequence would have sufficed for this purpose.

Conclusion

No claims are free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAMUEL C. WOOLWINE whose telephone number is (571)272-1144. The examiner can normally be reached on Mon-Fri 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Samuel Woolwine/
Primary Examiner, AU 1637